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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
EPPS, JANET L	

ART UNIT	PAPER NUMBER
1635	21

DATE MAILED: 07/25/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/601,997	KECK ET AL.	
	Examiner	Art Unit	
	Janet L. Epps-Ford, Ph.D.	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 May 2003* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *8-14 and 58-72* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *8-14 and 58-72* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *20* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

1. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

2. Claims 58-69 were previously withdrawn from consideration by the examiner as being drawn to a non-elected invention. However, since Applicants have amended these claims to read upon the elected invention, these claims will now be joined with the elected invention.

Claim Rejections - 35 USC § 102

3. Claims 8-14 remain rejected, and claims 58-72 are rejected under 35 U.S.C. 102(e) as being anticipated by Beach et al. (US Patent 6,255,071), for the reasons of record in the Office Action mailed 1-09-03.

4. Applicant's arguments filed 5-07-03 have been fully considered but they are not persuasive. Applicants traverse the instant rejection on the grounds that Beach et al. does not disclose every element of the claimed subject matter because Beach et al. does not: provide a method that assign a previously unknown function to a nucleic sequence present in a sample; design and prepare an oligonucleotide family containing related members of a known sequence with unknown function as described in the instant application; express the members of the aforementioned oligonucleotide family in a host cell; detect and analyze the phenotypic changes within the host cell; and assign a previously unknown function to the sample nucleic acid of known sequence based upon the observed phenotypic change.

Contrary to Applicant's assertions, the antisense methods of Beach et al. includes those methods, which do not rely on direct selection of a gene's function. These methods can successfully be utilized to identify sequences that affect gene function even in the absence of

knowledge regarding such function, e.g., in instances where the phenotype of a loss-of-function mutation within a gene is unknown (col. 22, lines 30-39). Beach et al. also state that single gene antisense libraries can be used to create targeted functional knockouts of individual genes. This can be accomplished without prior knowledge of the phenotype of the knockout by creating an indirect selection for loss of gene function using a quantifiable marker gene, see also Example 15, col. 48). As stated in the prior Office Action, Beach et al. describes antisense methods for gene cloning which can include a method for identifying new nucleic acid sequences based upon the observation that loss of function of an unknown gene produces a particular phenotype, and can comprise, for example, (a) infecting a cell with a retrovirus derived from a GSE-producing retroviral vector containing a test nucleic acid sequence, or, alternatively, transfecting such a cell with a vector of the invention containing a test nucleic acid sequence, wherein, upon infection, an integrated provirus is formed, or, depending on the vector, an episomal sequence is established, and the test nucleic acid is expressed; and (b) assaying the infected cell for a change in the phenotype, so that new nucleic acid sequences may be isolated based upon the observation that loss of an unknown gene produces a particular phenotype(col. 24, lines 17-34). This method comprises assigning a function to a particular nucleic acid sequence that was not previously known prior to screening by observing phenotypic changes in cells as a result of transfecting said cells with a test nucleic acid.

Moreover, Beach et al. teach a method that comprises assigning a function to unknown nucleic acid sequences. This method comprises transfecting cells with cDNA libraries and assaying for a phenotypic change in the cells. In one example, Beach teaches that factors that promote the survival of stem cells can be assayed for by transfecting, for example, hematopoietic

stem cells with cDNA libraries derived from stromal cells, and assaying for surviving infected cells, wherein selection for surviving cells may result in the identification of those cells with carry cDNA encoding factors necessary for survival. (col. 27, lines 50-67).

Moreover, as stated in the prior Office Action, Beach et al. teach an in vitro screen for genes that can induce telomerase activity in normal human mammary epithelial cells (HMEC). In this method, pools of cDNAs comprising from 100--100 clones each (either in the sense orientation or in the *antisense orientation* in the MaRXIIg vector series) are introduced into HMEC cells. These are selected for expression of cDNA and then used to prepare lysates for the assay of telomerase activity. Cell lysates are tested using a highly sensitive telomerase assay, which is capable of detecting two telomerase-positive cells among 20,000 telomerase-negative cells. Those pools, which upon infection cause the induction of telomerase activity in HMEC cells, are subdivided into smaller pools. Sub-pools are again used for the infection of HMEC cells, which are subsequently assayed for telomerase activity. Successive rounds of this procedure can identify an individual clone that acts as an inducer of the telomerase enzyme. Such a clone could represent a direct regulator of the enzyme itself or of the expression of a component of the enzyme. Alternatively, such a clone could act as a regulator of cell mortality. Changes induced by the expression of such a clone could induce the telomerase enzyme as only one aspect of a more global change in cellular behavior (col 48, line 54, to col. 49, line 20). In the case where the cDNA is introduced in antisense orientation (see col. 48, line 66), it is possible that the expression of this antisense construct produces a transcript in and of itself functions as an inducer that inhibits the ability of a suppressor of telomerase enzyme activity. Therefore in this example, alteration of gene function is associated with the expression of or the

level of synthesis of the telomerase enzyme, which is a normal physiological and biological function associated with mammalian cells. Prior to this in vitro screen, the function or the phenotype produced by the cDNA molecules in the assay was unknown. Function was assigned after observing phenotypic changes associated with cells transfected with cDNAs in either the sense or antisense orientation.

Contrary to Applicants assertions Beach et al. does provide a method that assign a previously unknown function to a nucleic sequence present in a sample; design and prepare an oligonucleotide family containing related members of a known sequence with unknown function as described in the instant application; express the members of the aforementioned oligonucleotide family in a host cell; detect and analyze the phenotypic changes within the host cell; and assign a previously unknown function to the sample nucleic acid of known sequence based upon the observed phenotypic change, as described in the above methods involving the transfection of nucleic acids into cells and the assaying for phenotypic changes associated with the transfected cells, and the assigning of function to the transfected nucleic acids as a result of these phenotypic changes, as in the example involving antisense based methods.

In regards to newly amended claims 58-72, Beach et al. disclose: (instant claim 58) genetic suppressor element producing vectors that can be utilized in conjunction with antisense-based functional inactivation methods. These vectors may be retroviral vectors, and may comprise a sense or antisense cDNA, in the case of the antisense cDNA, the sense strand of the vector would produce an antisense transcript (col. 12, lines 48-67). These vectors may also comprise ribozymes, which comprise flanking sequence and a catalytic core (col. 12-14). The vectors of Beach et al. may also comprise transcriptional regulatory sequences from adenovirus

Ad2 VA RNA (col. 13, lines 28-34). Moreover, the methods of Beach et al. comprise the analysis of libraries of cells transfected with the constructs of the Beach et al. invention, see for example col. 41-42, example 11. These libraries allow for the screening of multiple sequences, and thus can be considered a high-throughput screening method.

Conclusion

5. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

6. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Janet L. Epps-Ford, Ph.D. whose telephone number is 703-308-8883. The examiner can normally be reached on M-T, Thurs-Fri, 8:30AM-6:30PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, John L. LeGuyader can be reached on 703-308-0447. The fax phone numbers for the organization where this application or proceeding is assigned are 703-305-3014 for regular communications and 703-746-5143 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Janet L. Epps-Ford, Ph.D.
Examiner
Art Unit 1635

JLE
July 24, 2003

SEAN McGARRY
PRIMARY EXAMINER
1635